Please add the following new claims:

16. (New) The oil adjuvant vaccine of claim 1, wherein the outer aqueous phase comprises 1 - 5 wt% of the polyethylene glycol derivative of the formula (I).

B2

17. (New) The oil adjuvant vaccine of claim 1, wherein the polyethylene glycol derivative of the formula (I) has a molecular weight of 3,000 - 9,000.

REMARKS

The Present Invention

The present invention is directed to a novel W/O/W type oil adjuvant vaccine comprising (a) an inner aqueous phase comprising a biologically acceptable and effective amount of antigen, (b) an oil component phase which is in a liquid state at a temperature in the range of 15-25 °C, and (c) an outer aqueous phase comprising 0.5 - 20 wt% of a polyethylene glycol derivative having a molecular weight of 400 - 20,000, which is represented by formula (I), wherein R^1 and R^2 may be the same or different and each is a hydrogen atom or alkyl having 1 to 4 carbon atoms and n is a polymerization degree. The inner aqueous phase is discontinuous and suspended in the oil component phase, and the oil component phase is discontinuous and suspended in the outer aqueous phase.

The oil adjuvant vaccine differs from the oil adjuvant vaccines known in the prior art by the addition of a particular amount of a particular polyethylene glycol (PEG) derivative with specific characteristics to the outer aqueous layer. The addition of this PEG derivative to the outer aqueous phase has the surprising and unexpected benefit of reducing the viscosity of the vaccine, irrespective of the components of the inner aqueous phase (e.g., the antigen) (see, e.g., page 11, line 14 - page 12, line 6). Additionally, the stability of the vaccine formulation is improved by the addition of the particular PEG derivative to the outer aqueous layer (see, e.g., page 11, line 14 - page 12, line 6). These improvements over the oil adjuvant vaccines of the prior art increase the diffusing performance of the vaccine in the body and reduce adverse side effects, such as topical response and residual vaccine at the injection site (see, e.g., page 11, line 14 - page 12, line 6).

The Pending Claims

Claims 1-17 are currently pending.

The Amendments to the Claims

Claim 1 has been amended to point out more particularly and claim more distinctly the present invention. Specifically, claim 1 has been amended to recite further characteristics of the components of the W/O/W oil adjuvant vaccine as described in the specification at page 4, line 37, through page 5, line 6 and page 8, lines 31-36. Claims 16 and 17 are new., and are supported by the specification at page 10, line 16-21. No new matter has been added by way of these amendments. Separate documents setting forth the amendments to the claims, as well as the text of all of the pending claims as amended are enclosed.

The Office Action

The Office has rejected claims 1-15 under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. Reconsideration of this rejection is hereby requested.

Discussion of Rejection

The Office contends that the specification disclosure is insufficient on how to make and how to use all of the vaccines that would be encompassed by the claims (Office Action, page 2).

Applicants thank Examiner Ewoldt for granting an Examiner interview on February 5, 2003 to discuss the present invention with applicants' representatives John Kilyk, Jr. and Rachel J. Potempa. As discussed in the telephone interview, the use and method of preparing W/O/W oil adjuvant vaccines was known in the prior art at the time of the invention. However, the W/O/W oil adjuvant vaccine of the present invention differs from the W/O/W oil adjuvant vaccines of the prior art by the addition of a particular polyethylene glycol (PEG) derivative with specific characteristics to the outer aqueous phase. The addition of this particular PEG derivative to the outer aqueous phase has the surprising and unexpected benefit of reducing the viscosity of the vaccine, irrespective of the components of the inner aqueous phase (e.g., the antigen) (see, e.g., page 11, line 14 - page 12, line 6). Additionally, the stability of the vaccine formulation is improved by the addition of this particular PEG derivative to the outer aqueous layer (see, e.g., page 11, line 14 - page 12, line 6). These improvements over the oil adjuvant vaccines of the prior art increase the diffusing performance of the vaccine in the body and reduce adverse side effects, such as topical response and residual vaccine at the injection site (see, e.g., page 11, line 14 - page 12, line 6).

The Examples section of the specification of the present application contains Examples 1-9 describing vaccines 1-9. Vaccines 1-9 are W/O/W oil adjuvant vaccines

comprising a PEG derivative of the type set forth in the pending claims in the outer aqueous phase as recited in the pending claims. The Examples section also contains Comparative Examples 1-7 describing vaccines 10-16. Vaccines 10-16 are W/O/W oil type adjuvant vaccines which do *not* contain a PEG derivative in the outer aqueous layer. The vaccines in Examples 1-9 and Comparative Examples 1-7 are produced in essentially the same manner, with the exception of the addition of a PEG derivative to the outer aqueous layer in the vaccines of Examples 1-9. An overview of the preparation of W/O/W oil type adjuvant vaccines is summarized in Figures A – D (attached hereto).

For example, Example 1 describes the method of producing vaccine 1. As summarized in Figure A and described on page 14, line 22, through page 15, line 15, of the specification, an antigen suspension was added to a mixture of ethyl oleate, sorbitan sesquioleate, polyoxyethylene(40) hydrogenated castor oil, and an aqueous solution of sodium glutamate and sorbitol (see specification Table 1, W/O-1). The composition was stirred at 12,000 rpm for 5 minutes to create a W/O type emulsion. A mixture of polyoxyethylene(60) hydrogenated castor oil, polyoxyethylene(196) polyoxypropylen(67) glycol, Macrogol 6000 (a PEG derivative), and phosphate buffered saline (see specification Table 3, outer aqueous phase 1) was combined with the W/O type emulsion and stirred at 9,000 rpm for 5 minutes to create the W/O/W oil adjuvant vaccine 1 of the present invention.

The W/O/W oil adjuvant vaccine 10 of Comparative Example 1 was prepared in the same way and with the same components as in Example 1, except that no Macrogol 6000 (a PEG derivative) was added to the outer aqueous phase (see specification Table 4, outer aqueous phase 5). The production method and components of W/O/W oil adjuvant vaccine 10 of Comparative Example 1 are summarized in Figure B and at page 17, lines 10-13, of the specification.

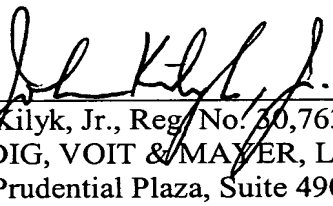
The inclusion of the PEG derivative in vaccine 1 of Example 1 is the only difference between vaccine 1 of Example 1 and vaccine 10 of Comparative Example 1, yet this difference results in drastic differences in performance of the vaccine. For example, vaccine 1 of Example 1 (representative of similar vaccines of the present invention) has a much lower viscocity than vaccine 10 of Comparative Example 1 (representative of the vaccines of the prior art) (see specification Table 9). Additionally, as is apparent from Table 6 of the specification, the effectiveness (PD_{50}) of vaccine 1 is about 5 times greater than the effectiveness of vaccine 10. The lower viscocity and increased effectiveness of the vaccines of the present invention are improvements over the same type of vaccines same type of known in the prior art.

As detailed in the above paragraphs, the method of preparation and components of the W/O/W oil type adjuvant vaccines of the present invention are essentially the same as those known in the prior art, with the exception of the addition of a PEG derivative to the outer aqueous layer. Thus, accompanied by what is known in the prior art, the disclosure in the specification contains a sufficient written description for an ordinarily skilled artisan to make and use the vaccines embodied by the pending claims. For those reasons, the section 112, first paragraph, rejection should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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Date: February 27, 2003

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I hereby certify that this "Response to Office Action" and all accompanying documents are being deposited with the United States Postal Service "Express Mail Post Office To Addressee" Service under 37 CFR 1.10 on the date indicated below and is addressed to: Commissioner for Patents, Washington, D.C. 20231.

Rick D. Madsen		February 27, 2003
Name of Person Signing	Signature	Date